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Consensus Conference on Cancer Registration of Brain and Central Nervous System Tumors[1]

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The passage of Public Law 107-260, the Benign Brain Tumor Cancer Registries Amendment Act, in October 2002 has made the collection of all primary brain tumors a reality. However, at the first Consensus Conference on Brain Tumor Definition for Registration in 2002, and during the development of training materials for benign brain tumor collection, several issues were identified that were tabled for future discussion. These and other issues were addressed at the subsequent 2003 Consensus Conference on Cancer Registration of Brain and Central Nervous System Tumors, at which the Central Brain Tumor Registry of the United States facilitated a discussion among epidemiologists, neurosurgeons, and neuropathologists. Multidisciplinary consensus was reached on four points, for which the following recommendations were made: (1) amend the histology coding scheme for cysts and tumor-like lesions that currently have a code in the third edition of the International Classification of Disease for Oncology (ICDO), (2) collect data on all instances of specific cysts and tumor-like lesions that are located in brain and other CNS sites but currently lack ICDO codes, (3) establish a new ICDO topography site for skull base tumors for the brain and CNS, and (4) collect data on genetic syndromes in patients diagnosed with brain or CNS tumors. We view this conference as part of a continuing process. Because classification of primary intracranial and other CNS tumors is dynamic, and the registration and coding of these tumors will need to be periodically reviewed. *Neuro-Oncology 7, 196–201, 2005 (Posted to Neuro-Oncology [serial online], Doc. 04-050, February 11, 2005. URL http://neuro-oncology.mc.duke.edu; DOI: 10.1215/S115285170400050X)*

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[3] Abbreviations used are as follows: CBTRUS, Central Brain Tumor Registry of the United States; IARC, International Agency for Research on Cancer; ICDO-3, International Classification of Diseases for Oncology, third edition; NAACCR, North American Association of Central Cancer Registries; NCCCS, National Coordinating Council for Cancer Surveillance; NPCR, National Program of Cancer Registries; SNOMED, Systematized Nomenclature of Medicine of the College of American Pathologists.

The registration of tumors of the central nervous system has been a concern for the brain tumor clinical, research, and patient communities as well as for the cancer surveillance community. In 1998, the Brain Tumor Working Group was appointed by the National Coordinating Council for Cancer Surveillance (NCCCS)[3] to investigate the surveillance of primary intracranial and CNS tumors (BTWG, 1998). The NCCCS is the umbrella organization that coordinates cancer surveillance activities within the United States through communication and collaboration among major national cancer organizations, ensuring that the needs of cancer patients and the communities in which they live are fully served, that scarce resources are maximally used, and that the burden of cancer in the United States

is adequately measured and ultimately reduced (Greene, 1997). Its members include the Centers for Disease Control's National Program of Cancer Registries (NPCR), the National Cancer Institute's Surveillance, Epidemiology, and End Results program, the American College of Surgeons' Commission on Cancer's National Cancer Data Base, and the National Center for Health Statistics. In addition, the American Cancer Society (ACS), the National Cancer Registrars Association (NCRA), the Armed Forces Institute of Pathology (AFIP), and the North American Association of Central Cancer Registries (NAACCR) are members. Development of uniform standards, uniform coding rules, and uniform content are goals of the NCCCS. Because the Central Brain Tumor Registry of the United States (CBTRUS) provides statistical data on all primary brain tumors from state cancer registries that collect data on benign and uncertain as well as malignant brain tumors, the NCCCS decided to access its members' collection of these data to ensure uniformity of standards.

The recommendations formulated by the NCCCS Brain Tumor Working Group included reaching an agreement on the standard definition for collecting precise data for all primary intracranial and CNS tumors. To further this goal, CBTRUS convened the Consensus Conference on Brain Tumor Definition for Registration (Consensus Conference I) in November 2000, with participants representing surveillance organizations belonging to the NCCCS and those belonging to clinical, research, and professional brain tumor organizations (McCarthy et al., 2002). Consensus was reached on a standard definition for collecting data on primary brain tumors based on site, as follows (codes for International Classification of Diseases for Oncology [ICDO] are given in parentheses after each site): Primary intracranial and CNS tumors are all primary tumors occurring in the following sites, irrespective of histologic type or behavior: meninges (C70.0–70.9); brain (71.0–C71.9); spinal cord, cranial nerves, and other parts of the central nervous system (72.0–C72.9); pituitary (75.1); craniopharyngeal duct (C75.2); and pineal gland (C75.3). This standard definition was used in the Benign Brain Tumor Cancer Registries Amendment Act, which was passed two years later as Public Law 107-260 (2002). Even though Public Law 107-260 only mandated collection of benign and uncertain brain tumors having ICDO codes by the registries participating in the Center for Disease Control's NPCR, all members of NCCCS voluntarily agreed to incorporate these tumors into their collection practices for brain tumors.

Two committees were appointed to address implementation issues: NCCCS appointed the Brain Tumor Working Group II to formulate guidelines for implementation, and the NAACCR appointed the Registry Operations Committee Benign Brain Tumor Sub-Committee to address the practical application of these guidelines. In June 2003, the NAACCR Standards Committee accepted the Brain Tumor Working Group II and Registry Operations Committee Benign Brain Tumor Sub-Committee's guidelines for benign and uncertain brain tumors and incorporated them into its Uniform Standards. In September 2003, NPCR sponsored a training workshop for benign brain tumor collection, and according to Public Law 107-260, surveillance organizations belonging to NCCCS began collecting benign brain tumors in January 2004 using established NAACCR standards.

Rationale

During the process of reaching consensus on a standard definition for brain tumor registration and formulating implementation guidelines, concerns surfaced about the rules that guide the collection and reporting of all primary brain tumors. Consequently, the Brain Tumor Working Group II and the Registry Operations Committee Benign Brain Tumor Sub-Committee worked in concert to help produce rules for the collection and reporting of benign brain tumors (NAACCR, 2003). Even though this was the committees' sole charge, they proposed changes to the rules that guide the collection and reporting of malignant brain tumors. These proposed changes have been referred to the Surveillance, Epidemiology, and End Results Site Histology Committee and have not been finalized at this time. However, issues regarding topography (site) code changes, the addition of brain-related cysts and tumor-like lesions, and the collection of data on genetic syndromes were beyond the scope of these work groups. The rationale for these proposed changes to data collection is outlined below.

The Benign Brain Tumor Cancer Registries Amendment Act stipulates that primary brain-related tumors located in the sites listed in the brain tumor site definition must also be listed in ICDO (Fritz et al., 2000; Public Law 107-260, 2002). Clinicians and researchers, especially neuropathologists, realized the full impact of this rule during implementation meetings for the collection of the benign brain tumors by state cancer registries. While many benign tumors, cysts, and tumor-like lesions occurring in brain-related sites are listed in the third edition of ICDO (ICDO-3) (Fritz et al., 2000), several brain-related cysts and tumor-like lesions deemed important by the brain tumor research and clinical community are listed only in the Systematized Nomenclature of Medicine (SNOMED) of the College of American Pathologists, and a few brain-related cysts and tumor-like lesions are not listed in either ICDO or SNOMED. As such, the brain-related cysts and tumor-like lesions not listed in ICDO would not be reported to the central cancer registries, and this exclusion would prevent an accurate population-based assessment of the distribution of these conditions.

The addition of a new site classification for brain and CNS tumors had been suggested at Consensus Conference I (McCarthy et al., 2002). Under the current ICDO-3 site classification scheme, meningiomas have three site codes: C70.0 (Cerebral Meninges), C70.1 (Spinal Meninges), and C70.9 (Meninges, NOS) (Fritz et al., 2000). Meningiomas that are given more specific site classifications by pathologists, neuropathologists, or clinicians are often coded to the NOS (C70.9) category. A specific site code to capture tumors found in the cav-

Table 1. Cysts and tumor-like lesions with ICDO-3 morphology codes*

Cyst	ICDO
Dermoid cyst, dermoid, squamous epithelial cyst	9084/0
Rathke pouch tumor	**9350/1 (C75.1)**
Consensus that this should not be classified with Craniopharyngioma and should have its own classification code. (See Rathke cleft cyst in Table 2.)	
Craniopharyngioma	9350/1 (C75.2)
Craniopharyngioma, adamantinomatous	9351/1 (C75.2)
Craniopharyngioma, papillary	9352/1 (C75.2)
Meningiomatosis, NOS	9530/1
Granular cell tumor, choristoma, pituicytoma, granular cell tumor of the neurohypophysis, granular cell tumor of the infundibulum, granular cell myoblastoma	9580/0
Granular cell neuroma, Abrikossoff tumor	9580/0
Granular cell tumor, malignant, granular cell, myoblastoma, malignant	9580/3
Granular cell tumor in sellar region, follicular cyst of the pituitary gland	9582/0 (C75.1)

* Fritz et al., 2000

ernous sinus, petrous bone, sphenoid wing, and other skull base sites was recommended, because the capability to collect information on tumors in this site would be beneficial for clinical research.

Several genetic conditions or syndromes are associated with increased predisposition to the development of certain brain neoplasms. Many of these syndromes, such as neurofibromatosis 1 and neurofibromatosis 2, are associated with the occurrence of numerous primary brain tumors in each affected patient; others, such as hereditary nonpolyposis colon cancer (Turcot's syndrome), can be associated with the early onset of malignant brain tumors (Kleihues and Cavenee, 1997; Lindor and Greene, 1998; McLendon and Tien, 1998; Taylor et al., 2001). Knowledge of the incidence and the personal and financial impact of these inherited syndromes in individuals with brain and CNS tumors is markedly incomplete because it is based on individual hospital case records not captured in statewide data. Although it is likely that initially the data collected on inherited syndromes may not be complete because of incomplete information in the medical records or incomplete data abstraction, the addition of this variable to the reporting requirements would allow investigators to begin to estimate the impact of inherited syndromes in these individuals. Eventually, the standardization of data collection rules and the increased use of this information in diagnosis and treatment will result in the improvement of the accuracy and completeness of these data.

Collection of data on syndromes also provides a resource for researchers to learn about mutations that are common to these syndromes through special study investigations. Information on mutations occurring in these neurogenetic syndromes can contribute to the body of knowledge concerning tumorigenesis of intracranial and other CNS tumors. For example, detailed molecular analyses of the genetic syndromes associated with brain and CNS tumors have "led to the important finding that the sequential loss of genetic material plays a significant role in tumorigenesis" (Thapar et al., 1995). Mutations in tumor suppressor genes associated with specific familial syndromes have also been found in sporadic tumors, such as mutations of the *NF2* gene in sporadic meningiomas (Bigner et al., 1998). Therefore, identifying the role of these tumor suppressor genes in tumorigenesis has implications not only for familial disease, but for sporadic tumors as well. Collection of data on inherited syndromes in cancer registries would provide researchers with a valuable resource to obtain information on the genetics of brain and CNS tumors.

Methods

A comprehensive review of ICDO-3 was conducted to identify brain-related cysts and tumor-like lesions currently collected by the central cancer registries (Table 1; Fritz et al., 2000). After a literature review, a review of SNOMED codes, and discussions with researchers, clinicians, and neuropathologists (Appendix), a comprehensive list of brain-related cysts and tumor-like lesions that do not have ICDO-3 codes was developed.

Results

In November 2003, CBTRUS facilitated the Consensus Conference on Cancer Registration of Brain and Central Nervous System Tumors (Consensus Conference II). Representatives belonging to clinical and research organizations met in Keystone, Colorado, during the Society for Neuro-Oncology Annual Meeting to review the registration of cysts and tumor-like lesions of the brain and the entire CNS, to consider a topography code in ICDO for skull base tumors, and to agree on a list of genetic

Table 2. Proposed new ICDO morphology codes for cysts and tumor-like lesions*

Cyst	Proposed ICDO Code
Rathke cleft cyst, **Rathke's pouch tumor**, Rathke's pouch cyst, embryonic cyst	9353/0
Neuroglial cyst, ependymal cyst, glio-ependymal cyst	9395/0
Pineal cyst, glial cyst of the pineal body	9395/0 (C75.3)
Enterogenous cyst, endodermal cyst	9354/0
Epidermoid cyst, squamous epithelial cyst, congenital keratin cyst	9086/0
Epidermoid carcinoma	9086/3
Colloid cyst of the third ventricle, colloid cyst, parahypophyseal cyst, congenital colloid cyst	9396/0
Hypothalamic neuronal hamartoma, hypothalamic hamartoma, hamartoblastoma	9494/0
Choroid plexus cyst	9397/0
Nerve root cyst, perineurial cyst, Tarlov cyst	9572/0

*It was agreed that both of the following lesions should be collected and should be grouped with the meningiomas. However, no separate codes are available.

- Meningioangiomatosis
- Arachnoid cyst, leptomeningeal cyst

Agreement was also reached that (1) the current ICDO-3 histology codes 9533/0 (Psammomatous meningioma) and 9534/0 (Angiomatous meningioma) could be combined into 9530/0 (Meningioma, NOS) and (2) the current ICDO-3 histology code 9535/0 (Hemangioblastic meningioma [obs]; angioblastic meningioma [obs]) could be eliminated.

syndromes associated with CNS tumors. Consensus was achieved on four recommendations.

Recommendation 1

The list of cysts and tumor-like lesions of the brain and CNS that currently are coded in ICDO-3 was reviewed. Recommendation for a change to the existing morphology coding scheme, specifically that Rathke pouch tumor be given a separate ICDO code rather than be combined with craniopharyngioma (9350/1), was suggested (Table 1).

Recommendation 2

The collection of additional selected cysts and tumor-like lesions found in brain-related sites but currently lacking ICDO codes was recommended. A list of proposed ICDO codes for these cysts and tumor-like lesions is presented in Table 2. Participants in the 2003 Consensus Conference II reviewed brain-related cysts and tumor-like lesions having either SNOMED but not ICDO codes or neither SNOMED nor ICDO codes, and they recommended the assignment of ICDO codes to these cysts and tumor-like lesions of the CNS. The proposed codes are based on the participants' review of current ICDO-3 coding assignments (Fritz et al., 2000).

Table 3. Brain and other CNS tumors to be assigned to C70.2, Skull Base Tumors, a proposed new ICDO topography code

Foramen magnum
Meninges of the skull base
Parasellar (moved from C72.9)
Suprasellar (moved from C71.9)
Sellar
Cavernous sinus
Clivus
Meckel's cave
Petrous bone
Sphenoid wing

Recommendation 3

The addition of a new ICDO topography code for skull base tumors (C70.2) was recommended. The proposed code is based on the review by the consensus conference participants of current topography codes listed in ICDO-3 and the importance of accurately capturing tumors of the nervous system with increased topographic specificity. Recommendations for changes to existing coding are listed in Table 3.

Recommendation 4

The collection of data on genetic syndromes in persons diagnosed with tumors of the brain and CNS was recommended (Table 4). Participants in Consensus Con-

Table 4. Genetic syndromes associated with brain and central nervous system tumors

Neurofibromatosis I (von Recklinghausen's disease; peripheral neurofibromatosis)
Neurofibromatosis II (bilateral acoustic neurofibromatosis; central neurofibromatosis)
Von Hippel–Lindau disease
Tuberous sclerosis (tuberous sclerosis complex)
Gorlin syndrome (nevoid basal cell carcinoma syndrome)
Li-Fraumeni syndrome (p53 syndrome)
Heritable or bilateral (familial or sporadic) retinoblastoma
Familial adenomatous polyposis (adenomatous polyposis coli; Turcot syndrome)
Hereditary nonpolyposis colorectal carcinoma syndrome (Lynch cancer family syndrome; Turcot syndrome)
Carney's complex
Cowden syndrome (multiple hamartoma syndrome)
Multiple endocrine neoplasia type I (Wermer syndrome)

ference II recommended that the NAACCR Uniform Data Standards Benign Brain Tumor Sub-committee consult with the NCCCS to discuss petitioning the Uniform Data Standards Committee to collect data on these genetic syndromes for brain and other CNS tumors.

Discussion

Recommendations 1–3 were sent to the International Agency for Research on Cancer (IARC), the designated agency of the World Health Organization responsible for maintaining, revising, and publishing the *International Coding of Diseases for Oncology* (Fritz et al., 2000), and will be considered by the IARC Editorial Committee for revisions to the next edition of ICDO. The implications of a new revision of ICDO are wide ranging. Cancer registries worldwide take great care when implementing changes because of issues of geographical comparability and trends over time (Letter from Sharon Whelan, IARC, January 9, 2004). The intent of Recommendations 1 and 2 was discussed with representatives from SNOMED at the American College of Pathology prior to Consensus Conference II, and discussions are ongoing. Recommendation 4 has been sent to the Uniform Data Standards Benign Brain Tumor Sub-committee, who will bring this issue to NCCCS. Because Consensus Conference II was restricted to discussions involving tumors of the brain and CNS, the collection of data on genetic syndromes related to CNS tumors will need to be addressed within the context of the collection of data on genetic syndromes related to all cancer sites.

Consensus Conference II is part of a continuum of meetings concerning issues affecting cancer registration of intracranial and other CNS tumors. Classification of these tumors is dynamic, and the registration and coding of these tumors will need to be continually reviewed. The interaction between the cancer registration community and the brain tumor clinical and research community as they worked together to implement the collection of benign brain tumors proved educational for both parties and continues to build on one of the recommendations of Consensus Conference I: to continue this joint effort between the surveillance and clinical communities. Meetings of this nature are part of the process of attaining the five-year research priorities set in 2000 by the Brain Tumor Progress Review Group, a joint effort of the National Cancer Institute and the National Institute of Neurological Disorders and Stroke (Brain Tumor Progress Review Group, 2000).

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